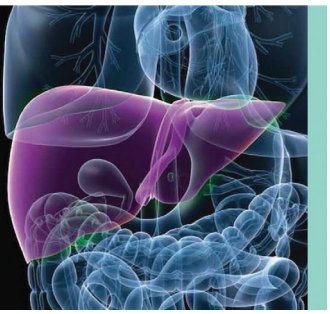

Developing an Evidence Base for the Delivery of Hepatitis B Virus Birth Dose Vaccination: An Evidence Map and Critical Appraisal of Systematic Reviews and Guidelines

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In 2016, the World Health Organization (WHO) set global goals for hepatitis B virus (HBV) elimination.[1] High coverage of HBV vaccination is a key pillar of HBV elimination because it is highly effective in preventing HBV infection and affords protection for at least 30 years.[2] Neonates born to HCV-infected mothers are at highest risk

Abbreviations: AAP, American Academy of Pediatrics; AASLD, American Association for the Study of Liver Diseases; ACIP, Advisory Committee on Immunization Practices; AGREE II, Appraisal of Guidelines for Research & Evaluation Instrument; AMSTAR, A Measurement Tool to Assess Systematic Reviews; CDC, Centers for Disease Control and Prevention; CRD, Centre for Reviews and Dissemination; HBIG, hepatitis B immunoglobin; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HepB-BD, birth dose of hepatitis B vaccine; HTA, Health Technology Assessment; IARC, International Agency for Research on Cancer; IDSA, Infectious Diseases Society of America; MoH, Ministry of Health; NACI, National Advisory Committee on Immunization; RCT, randomized controlled trial; SAGE, Strategic Advisory Group of Experts; SOGC, Society of Obstetricians and Gynaecologists of Canada; SR, systematic review; USPSTF, US Preventive Services Task Force; WHO, World Health Organization.

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for development of chronic infection. More than 90% of HBV-infected newborns remain infected, resulting in one in four dying of HBV-related liver disease in later life. Among infants born to hepatitis B surface antigen (HBsAg)-positive mothers, a birth dose of hepatitis B vaccine (HepB) reduces the risk for perinatal HBV transmission by 75% and by >90% when combined with other prevention strategies.[3]

Soon after hepatitis B vaccines became available in the early 1980s, a small number of countries began to vaccinate infants beginning soon after birth. In 2009, the WHO recommended all newborns receive a HepB-BD as soon as possible after delivery, preferably within 24 hours.[4] By 2015, a total of 97 countries had introduced the HepB-BD.[5] To reach the HBV elimination goal, WHO calls for HepB-BD coverage to reach 90% by 2030.[1] However, in 2017, only an estimated 43% of newborns received a timely HepB-BD.[6] HepB-BD coverage varies widely across regions and countries, but the lowest coverage is seen in sub-Saharan Africa, where as few as 1.3% up to 23% of newborns receive a timely dose of HepB-BD[7] and only 9% of countries have achieved 50% coverage of birth dose, the 2020 interim target.[8]

Previous systematic reviews and guidelines on HepB-BD have been of varying degrees of methodological quality. To identify and facilitate dissemination of the best available information on HepB-BD to policy makers and program managers, the Coalition for Global Hepatitis Elimination developed an evidence base that compiled existing systematic reviews and guideline documents on HepB-BD into one database and assessed their methodological approach. This report describes key characteristics of this evidence base (Supplement 1: Study Methods; Supplement 2: Database Search Strategies; Supplement 3: Grey Literature Search).

KEY FINDINGS

The literature search identified 856 references after duplicates were removed as presented in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Fig. 1). Full-text screening yielded 26 guideline documents, of which 12 represent the most recent iterations (Table 1) and 14 systematic reviews (including economic evaluations based on systematic reviews and narrative reviews; Table 2) met eligibility criteria for inclusion in the evidence base.[3-5,9-44] Only five guideline documents received a rating of more than 3 of 7 on the Appraisal of Guidelines for Research & Evaluation Instrument (AGREE) II scale (Fig. 2). Only one systematic review was appraised as high quality on the A Measurement Tool to Assess Systematic Reviews (AMSTAR) 2 instrument, while eight were of low or critically low quality (Fig. 3). Additional critical appraisal details are presented in Supplement 4. The following sections summarize the findings from the documents in the evidence base.

Effectiveness of HepB-BD

Vaccination has been established as effective for preventing HBV infection.[2] Whitford et al.[10] found adolescents and adults in birth cohorts with universal vaccination had 76% lower prevalence of hepatitis B infection, and those in targeted vaccination programs had 68% lower prevalence compared with unvaccinated cohorts. The earliest identified areas implementing targeted birth dose recommendations for infants born to HBsAg-positive mothers were Taiwan and the United States in 1984.[42,45] Taiwan went on to implement universal HepB-BD vaccination in 1986.[45] The United States first recommended universal birth dose vaccination for infants in 1991, when targeted vaccination of high-risk groups was found to be ineffective at reducing the incidence of infection.[31] The WHO recommended universal birth dose vaccination in 2009.[4] Guidelines for HepB-BD administration were identified from organizations in six countries and three global or regional organizations.

Economic Evaluations

Several reviews found HepB-BD is a cost-effective option for preventing HBV infection.[11,12,17] Anderson et al.[12] estimated universal HepB-BD vaccination would prevent 1,930 cases of HBV infection per 10,000 children vaccinated, more than even a strategy of targeted HepB-BD vaccinations and a pentavalent combination vaccine at 6 weeks. Dionne-Odom et al.[11] found birth dose vaccination and completion of the vaccination series was the most cost-effective method of reducing HBV infection in sub-Saharan Africa.

Barriers to Achieving and Strategies to Increase Birth Dose Coverage

Several reviews also investigated barriers to achieving universal birth dose coverage and strategies to increase coverage.[13,15,16,20,21] Lack of education about vaccination and HBV, home births, and rural location were the

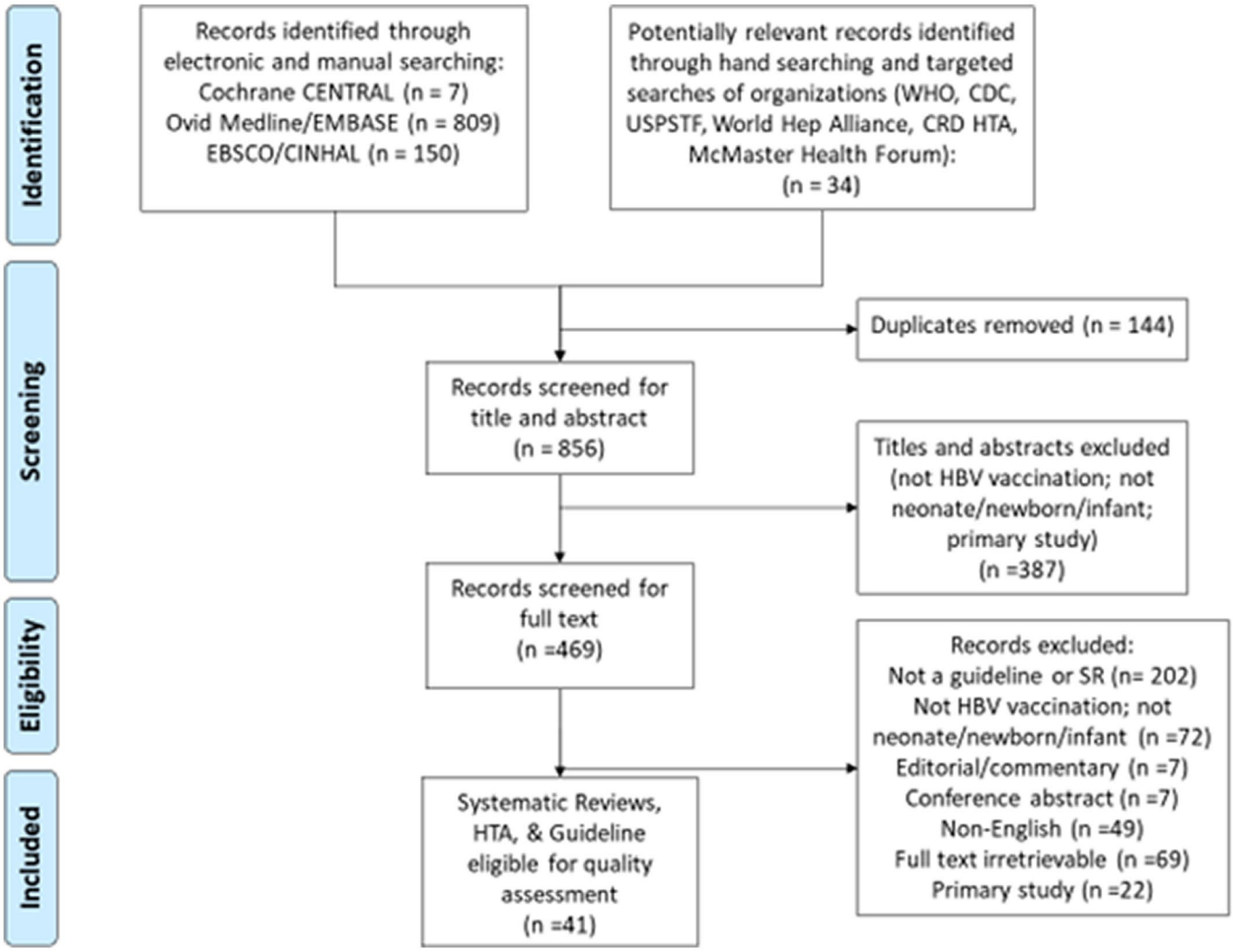

FIG 1 PRISMA study flow diagram.

TABLE 1. GUIDELINES INCLUDED IN CRITICAL APPRAISAL

Bibliography	Type	Country of Development	Guideline Funding Source	Guideline Development Organization(s)	AGREE II
Castillo et al. (2017)[23]	Clinical practice guideline	Canada	Professional society	SOGC	5/7
AAP Committee on Infectious Diseases and Committee on Fetus and Newborn (2017)[35]	Guidance	USA	Professional society	AAP	3/7
Terrault et al. (2018)[39]	Guidance	USA	Nonprofit	AASLD	4/7
Gardner et al. (2002)[26]	Guideline	USA	Professional society	IDSA	3/7
Government of Canada (2017)[44]	Guideline	Canada	Government	NACI	3/7
New Zealand Ministry of Health (2018)[40]	Guideline	New Zealand	Government	MoH	3/7
South Australia Maternal & Neonatal Community of Practice (2016)[38]	Guideline	Australia	Government	South Australia Maternal & Neonatal Community of Practice	2/7
Republic of Rwanda Ministry of Health (2015)[36]	Guideline	Rwanda	Government	MoH	2/7
Schillie et al. (2018)[3]	Recommendations	USA	Government	ACIP; CDC	6/7
Villain et al. (2015)[24]	Recommendations	European Union	Government	IARC	6/7
WHO (2017)[5]	Recommendations	Switzerland	Government	SAGE	4/7
Maponga et al. (2017)[22]	Recommendations	Global	Professional society; pharmaceutical	IAS	3/7

TABLE 2. SYSTEMATIC REVIEWS INCLUDED IN CRITICAL APPRAISAL

Bibliography	Type	Included Study Type	Countries of Included Studies	AMSTAR 2 Rating
Wright et al. (2018)[9]	Systematic review	Economic evaluation study	China, Gambia, India, Iran, Philippines, South Africa, Thailand	High
Whitford et al. (2018)[10]	Systematic review, meta-analysis	RCTs, cross-sectional	Australia, China, Fiji, Gambia, Italy, Taiwan	Moderate
Dionne-Odom et al. (2018)[11]	Systematic review	RCTs, prospective/retrospective cohort	Cameroon, Côte d'Ivoire, China, Democratic Republic of Congo, Ethiopia, Ghana, Indonesia, Israel, Laos, Papua New Guinea, Philippines, Sierra Leone, South Africa, Thailand, USA	Low
Anderson et al. (2018)[12]	Systematic review, decision analytic model	Prospective/retrospective cohort, cross-sectional	Cameroon	Low
Vedio et al. (2017)[13]	Systematic review	RCTs, prospective/retrospective cohort, cross-sectional, qualitative	Australia, Canada, United Kingdom, USA	Low
Chen et al. (2017)[14]	Systematic review, meta-analysis, network meta-analysis	RCTs	China, Hong Kong, India, New Zealand, Taiwan, Thailand	Moderate
Breakwell et al. (2017)[15]	Narrative review, systematic review	Cross-sectional	Cameroon, Gambia, Ghana, Nigeria, Senegal, South Africa, Tanzania	Critically low
Wang et al. (2016)[16]	Systematic review	Before-after, cluster RCT, cross-sectional, review	China	Moderate
La Torre et al. (2016)[17]	Systematic review	Economic evaluation study	Australia, Bulgaria, China, Germany, Iran, Ireland, Mozambique, Poland, South Korea, Taiwan, Thailand, USA, Vietnam	Low
Jin et al. (2014)[43]	Meta-analysis	RCTs	China	Low
Schonberger et al. (2013)[18]	Systematic review, meta-analysis	Prospective/retrospective cohort, cross-sectional	American Samoa, Brazil, Canada, China, Egypt, Iran, Italy, Micronesia, Mongolia, Nigeria, Saudi Arabia, Senegal, Spain, Taiwan, Thailand, USA	Moderate
Lee et al. (2006)[19]	Systematic review, meta-analysis	RCTs	China, Cuba, Hong Kong, India, Italy, Moldova, the Netherlands, New Zealand, Singapore, Taiwan, Thailand, Turkey, Uzbekistan, Vietnam	Moderate
WHO (2016)[20]	Systematic review	Prospective/retrospective cohort, cross-sectional	American Samoa, Australia, Brunei, Brazil, Cambodia, Cook Islands, China, Djibouti, Fiji, French Comoros, Gambia, Guam, Hong Kong, India, Indonesia, Iran, Iraq, Italy, Kiribati, Kuwait, Laos, Lebanon, Libya, Macao, Marianas Islands, Malaysia, Marshall Islands, Mayotte, Micronesia, Mongolia, Morocco, Nauru, New Caledonia, the Netherlands, Nigeria, Niue, Norway, Oman, Palau, Palestine, Papua New Guinea, Philippines, Polynesia, Puerto Rico, Qatar, Saudi Arabia, Singapore, Solomon Islands, South Korea, Switzerland, Syria, Tokelau, Tonga, Turkey, Tunisia, Tuvalu, United Arab Emirates, United Kingdom, USA, Vanuatu, Vietnam, Wallis Futuna	Critically low
Bhutta et al. (2005)[21]	Narrative review, systematic review	RCTs, prospective/retrospective cohort	Argentina, Bangladesh, Bolivia, Brazil, Burma, Cameroon, Chile, Colombia, China, Cuba, Democratic Republic of Congo, Denmark, Ecuador, Egypt, Ethiopia, Gambia, Ghana, Guatemala, Haiti, India, Indonesia, Israel, Kenya, Malawi, Mexico, Mozambique, Niger, Nepal, Nigeria, Pakistan, Papua New Guinea, Peru, Philippines, Saudi Arabia, Senegal, South Africa, Sweden, Swaziland, Taiwan, Tanzania, Thailand, Uganda, United Kingdom, USA, West Africa, Zambia, Zimbabwe	Low

most often identified barriers to HepB-BD. In a WHO review, home birth was identified as the largest barrier in the Western Pacific region, and living in rural areas was the largest barrier in the African region.[20] Bhutta et al.[21] found heat-stable vaccines and training for community health workers are cost-effective ways to address some of these barriers. In a review of barriers to vaccination among Chinese migrants, lack of knowledge was consistently found to be a barrier, but provider prompts and a dedicated infant vaccination service with follow-up were two interventions effective for increasing coverage.[13]

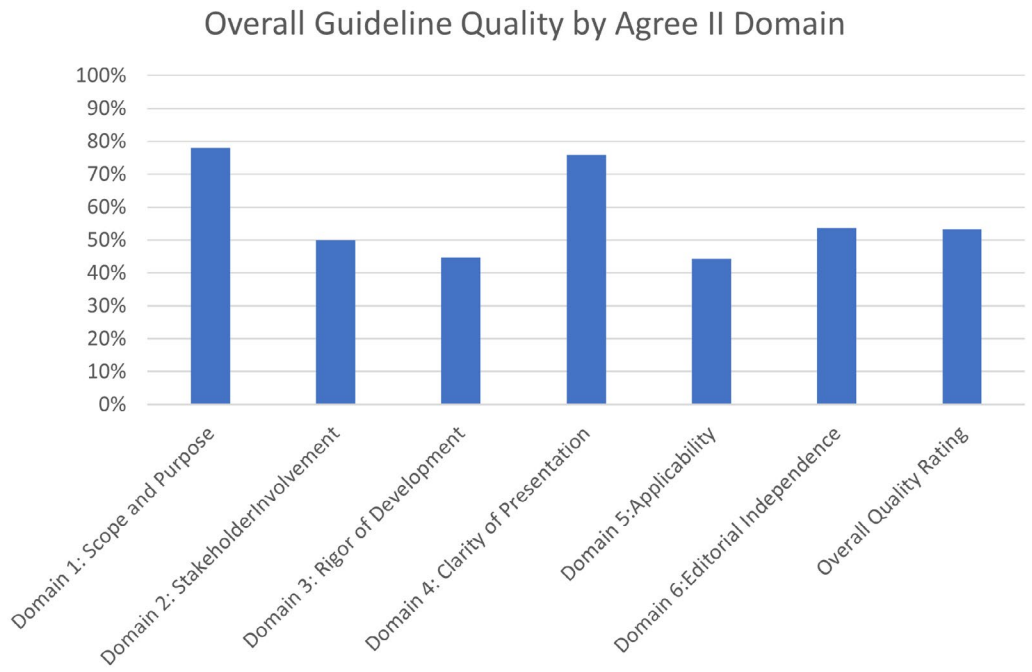

FIG 2 Overall guideline quality by AGREE II domain.

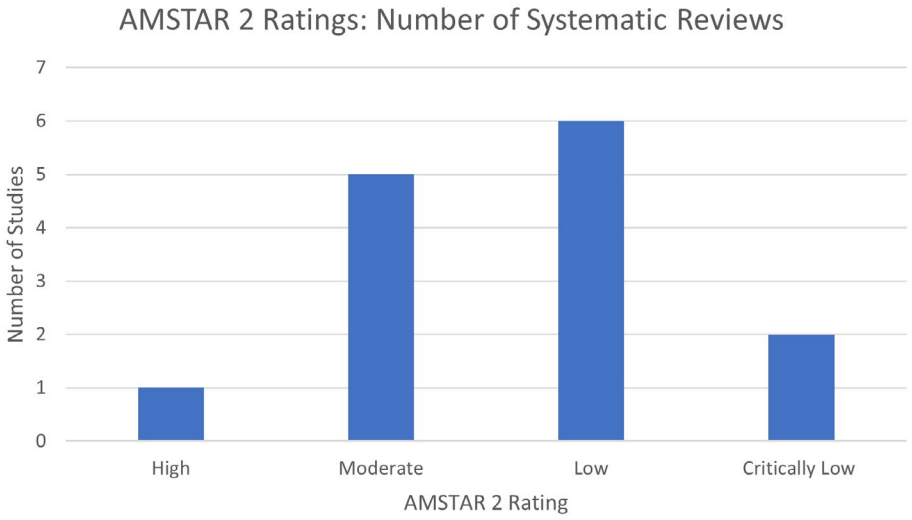

FIG 3 AMSTAR 2 ratings: Number of systematic reviews.

Perinatal Transmission

Perinatal transmission of hepatitis B is one of the most common methods of transmission,[2] and as such has been the focus of a number of reviews and guidelines. Four systematic reviews evaluated methods to reduce perinatal transmission, all finding HepB-BD is effective at reducing perinatal transmission.[11,14,19,43] Three reviews found combination with hepatitis B immunoglobin (HBIG) is more effective than the vaccine alone,[14,19,43] and two found antiviral treatment during pregnancy followed by HepB-BD is effective at reducing transmission.[11,14] In accordance with these studies, guidelines from the United States,[3,39] Canada,[23] Switzerland,[5] and New Zealand[40] recommend both HepB-BD and HBIG administration within 12 hours of birth for infants born to HBsAg-positive mothers. Rwanda recommends vaccination within 24 hours and HBIG within 14 days.[36]

CONCLUSION

This evidence base provides a database of available guidelines and systematic reviews pertaining to HepB-BD vaccination delivery, including relevant characteristics and a methodological quality rating. Based on the quality assessments performed, there is a need for additional high-quality evaluations of HepB-BD vaccination. Although guidelines included in this review were likely to describe the scope and intention, and transparently present the recommendations, many require increased transparency when reporting stakeholder involvement, guideline development methods, and implementation. The critical appraisal of systematic reviews of the evidence for timely delivery of HepB-BD vaccine demonstrated flaws in the methodological quality of the reviews. There are these limitations; however, the data and practical experience affirms HepB-BD vaccination and effectiveness in preventing transmission.

This evidence base contains all identified systematic reviews and guidelines referring to HepB-BD vaccination and is available at https://www.globalhep.org/evidence-base. It shows there are a variety of resources available with relevant information on the efficacy, cost-effectiveness, and barriers to implementing HepB-BD; however, methodological quality is lacking in many of these resources. Additional high-quality resources are necessary to inform delivery of infant vaccination against hepatitis B to ensure WHO targets for elimination can be met. This review identifies areas for improvement in the development of trustworthy guidelines and high quality systematic reviews. Future studies synthesizing the effectiveness of these interventions should improve the quality of the documents. The rigor of the evidence can help inform guidelines and policy development to implement programs to advance HepB-BD coverage, particularly in areas of low coverage and to meet global objectives.

CORRESPONDENCE

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